IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

MEDPOINTE HEALTHCARE INC.,	)	
	)	
Plaintiff,	)	C.A. No. 06-164 (SLR)
	)	
v.	)	
	)	
APOTEX INC. and APOTEX CORP.,	)	
	)	
Defendants.	)	

DEFENDANT APOTEX INC.'S AND APOTEX CORP.'S MOTION FOR ISSUANCE OF A LETTER OF REQUEST FOR MR. HELMUT HETTCHE

On January 26, 2007, the Court ruled that depositions sought to be taken by defendant Apotex Inc. and Apotex Corp. ("Apotex") of certain German witnesses shall be governed by the rules of the Hague Evidence Convention. See Order dated January 26, 2007 (D.I. 48). The reference to the Hague Evidence Convention meant those procedures found in the Hague Convention of 18 March 1970 On Taking Of Evidence Abroad In Civil Or Commercial Matters of which both the United States and Germany are signatories.

In lieu of the Court's January 26th Order, Apotex respectfully moves the Court for issuance of a Letter of Request to the designated German Central Authority to have Mr. Helmut Hettche, a German citizen, appear and answer questions under the rules of the Hague Evidence Convention. Mr. Hettche is the named inventor on U.S. Patent No. 5,164,194 ("'194 patent"), the patent-in-suit, and one of the witnesses at the center of the Court's January 26th Order. See Order dated January 26, 2007, ¶1 (D.I. 48). Plaintiff MedPointe Healthcare Inc. ("MedPointe") has already indicated that the German

witnesses, including Mr. Hettche, "have agreed to depositions under the rules of the Hague Convention." Id., ¶7, p. 4 (D.I. 48).

A Request For International Judicial Assistance Pursuant To The Hague Convention Of 18 March 1970 On Taking Of Evidence Abroad In Civil Or Commercial Matters for Examination of Mr. Helmut Hettche ("Letter of Request") is attached as Exhibit A. The Letter of Request complies with the format provided by the Hague Evidence Convention. In the interest of time and expense, Apotex has not yet translated the Letter of Request and associated exhibits into the German language pending any revisions that the Court may order to the Letter of Request. Once the Letter of Request is signed by the Court, Apotex will obtain certified German-language translations of the Letter of Request and associated exhibits and effect service upon the designated German Central Authority, in this instance the Präsident des Oberlandesgerichts Frankfurt.

The Letter of Request includes a list of questions (Tab 1) and exhibits (Tab 2) that are sought to be used in the examination of Mr. Hettche. The actual exhibits are not submitted with the Letter of Request but will be included with the service of the Letter of Request upon the designated German Central Authority. Many of the listed exhibits were produced by MedPointe in this action. Some of these original MedPointe exhibits were produced in the German language. Other exhibits were produced by Apotex in this action. For the benefit of United States counsel, Apotex will provide certified English translations of the German exhibits identified in the Letter of Request. Of course, exhibits in English will be translated to German for the benefit of the witness and German counsel.

Prior to submission of the Letter of Request, Apotex sent a copy to MedPointe for review so the parties could attempt to reach agreement as to the scope of discovery to be obtained under the Hague Convention. After receiving MedPointe objections to certain questions, Apotex amended or deleted individual questions. Apotex understands that MedPointe still objects to certain of the questions Apotex seeks to present to Mr. Hettche. Upon the filing of this motion, Apotex intends to contact the Court for direction on how to resolve these objections.

Apotex respectfully requests that the Court overrule MedPointe's objections and sign the Letter of Request as presented in Exhibit A and return the original to counsel for Apotex for translation and service upon the designated German Central Authority and counsel of record. It is submitted that any objections that may be raised with respect to the certified German translations can be handled by the parties, their respective German counsel and the German judicial authority designated to conduct the examination of Mr. Hettche.

Certification Pursuant to Local Rule 7.1.1. Defendants certify that their counsel has contacted counsel for Plaintiff about the attached motion and that Plaintiff is opposed to the relief sought in the motion.

Respectfully submitted,

POTTER ANDERSON & CORROON LLP

By: */s/ Kenneth L. Dorsney*

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WELSH & KATZ, LTD.
120 S. Riverside Plaza, 22nd Floor
Chicago, IL 60606
(312) 655-1500

Dated: April 12, 2007
787098 / 30136

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

CERTIFICATE OF SERVICE

I, Kenneth L. Dorsney, hereby certify that on April 12, 2007, the attached document was hand delivered on the following persons and was electronically filed with the Clerk of the Court using CM/ECF which will send notification of such filing(s) to the following and the document is available for viewing and downloading from CM/ECF:

Frederick L. Cottrell, III
Jameson A. L. Tweedie
Richards, Layton & Finger
One Rodney Square
P.O. Box 551
Wilmington, DE 19899

I hereby certify that on April 12, 2007, I have Electronically Mailed the foregoing document(s) to the following non-registered participants:

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EXHIBIT A

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

MEDPOINTE HEALTHCARE INC.,	)	
	)	
Plaintiff,	)	C.A. No. 06-164 (SLR)
	)	
v.	)	
	)	
APOTEX INC. and APOTEX CORP.,	)	
	)	
Defendants.	)	

REQUEST FOR INTERNATIONAL JUDICIAL ASSISTANCE PURSUANT TO THE HAGUE CONVENTION OF 18 MARCH 1970 ON TAKING OF EVIDENCE ABROAD IN CIVIL OR COMMERCIAL MATTERS

1.	Sender:	Hon. Sue L. Robinson Chief Judge United States District Court for the District of Delaware J. Caleb Boggs Federal Building 844 North King Street Wilmington, DE 19801-3519 (302) 573-6170
2.	Central Authority of Germany:	Präsident des Oberlandesgerichts Frankfurt Zeil 42 60313 Frankfurt am Main Germany
3.	Person to whom the executed request is to be returned:	Hon. Sue L. Robinson Chief Judge United States District Court for the District of Delaware J. Caleb Boggs Federal Building 844 North King Street Wilmington, DE 19801-3519 (302) 573-6170

4. In conformity with Article 3 of the Convention, the undersigned applicant has the honour to submit the following request:

5a. Requesting judicial authority:

United States District Court for the District of Delaware
J. Caleb Boggs Federal Building
844 North King Street
Wilmington, DE 19801

5b. To the competent authority of:

The Federal Republic of Germany, State of Hessen

6. Names and addresses of the Parties and their Representatives:

Plaintiff:

MedPointe Healthcare Inc.
265 Davidson Avenue
Somerset, New Jersey 08873
United States of America

Representative:

Gerald J. Flattman, Esq.
Kirkland & Ellis LLP
Citigroup Center
153 East 53rd Street
New York, New York 10022-4611
United States of America

Defendants:

Apotex, Inc.
380 Elgin Hills Road East
Richmond Hill, Ontario
Canada L4C 5H2

and

Apotex, Corp.
2400 North Commerce Parkway
Suite 400
Weston, Florida 33326
United States of America

Representative:

A. Sidney Katz
Robert B. Breisblatt
Welsh & Katz, Ltd.
120 South Riverside Plaza • 22nd Floor
Chicago, Illinois 60606-3912
United States of America

7.	Nature and purpose of the proceedings and summary of the facts:	MedPointe Healthcare Inc. ("MedPointe") is a U.S. pharmaceutical company that develops, markets and sells branded prescription drugs. Since August 16, 2002, MedPointe has been the sole owner of U.S. Patent No. 5,164,194 ("'194 patent") entitled "Azelastine Containing Medicaments." The '194 patent originally issued to Asta Pharma AG, as assignee, on November 17, 1992. Mr. Helmut Hettche is the sole named inventor on the '194 patent. MedPointe has sued Apotex, Inc. and Apotex, Corp. ("Apotex") for infringement of the '194 patent as a result of the filing of an Abbreviated New Drug Application with the United States Food and Drug Administration seeking to market and sell a generic nasal spray product containing 0.1% azelastine hydrochloride. Apotex has asserted non-infringement of the '194 patent. Apotex has also asserted that the '194 patent is invalid or unenforceable under the applicable United States Patent Laws.
8.	Evidence to be obtained or	Mr. Helmut Hettche can provide evidence on the matters set forth in the attached questionnaire. It is respectfully requested that an appropriate German judicial authority ask Mr. Hettche the list of attached questions.
9.	Identity and address of Person to be examined:	Mr. Helmut Hettche Romerstrasse #43 63128 Dietzenbach Germany
10.	Questions to be put to the person to be examined or statement of the subject matter about which he is to be examined:	Please see the attached questionnaire.
11.	Documents or other property to be inspected:	Any and all documents in the possession, custody or control of Mr. Hettche relating to the development or conception of azelastine containing medicaments.

12.	Any requirement that the evidence be given on oath or affirmation and any specific form to be used:	Mr. Hettche should be examined under oath or affirmation,or in the alternative, should be instructed of the consequences for giving untruthful answers under the laws of Germany.
13.	Special methods or procedure to be followed:	It is requested that: (1) the parties' representative and their designees, including local German counsel and interpreters be permitted to be present during the examination; (2) the representatives or their designees be permitted to request clarification or further elaboration of Mr. Hettche's answers to the questions posed; (3) the representatives or their designees be permitted to pose or submit for presentment to Mr. Hettche additional questions following presentment of the questions on the attached questionnaire; (4) if requested by Mr. Hettche, an attorney representing Mr. Hettche may be present and may participate on behalf of his client to the extent permitted by German law; (5) there be excluded from the examination, if permitted under German law, all persons other than the judicial officer conducting the examination of Mr. Hettche, the attorney representing Mr. Hettche, if any, the attorneys for the parties and their designees, interpreters, and other officials of the German court normally present during such proceedings. It is respectfully requested that the judicial proceeding be scheduled in Frankfurt am Main. In addition, it is requested that Mr. Hettche, who lives in Dietzenbach, be requested to travel to Frankfurt am Main for the judicial proceeding. Apotex intends to request that counsel representing Mr. Hettche voluntarily agree to attend a judicial proceeding scheduled in Frankfurt am Main.

14.	Request for notification of the time and place for execution of the Request and the identity and address of any person to be notified:	Please notify the following persons by mail and telefax when and where the examination is to be conducted: Robert B. Breisblatt, Esq. Welsh & Katz, Ltd. 120 South Riverside Plaza • 22nd Floor Chicago, Illinois 60606-3912 United States of America Tel. No.: (312) 655-1500 Fax No.: (312) 655-1501 Gerald J. Flattman, Esq. Kirkland & Ellis LLP Citigroup Center 153 East 53rd Street New York, New York 10022-4611 United States of America Tel. No.: (212) 446-4800 Fax No. (212) 446-4900 Joseph M. O'Malley, Jr., Esq. Bruce M. Wexler, Esq. Paul Hastings Park Avenue Tower 75 E. 55th Street First Floor New York, New York 10022 Tel. No.: (212) 318-6090 Fax No.: (212) 230-7712
15.	Request for attendance or participation of judicial personnel of the requesting authority at the execution of the Letter of Request:	None.
16.	Specification of privilege or duty to refuse to give evidence under the law of the State of Origin:	Mr. Hettche may refuse to answer any question propounded if such answer (1) would subject him to a real and appreciable danger of criminal liability in the United States, or (2) would disclose a confidential communication between him and his attorney or former attorney. In some cases, it may be the party rather than the witness who may

hold the privilege. In addition, an attorney may assert a privilege on behalf of a client with respect to a question propounded to Mr. Hettche. However, Mr. Hettche should respond to the question if he can do so without revealing the content of the privileged communication. If a privilege is asserted, Mr. Hettche is required to reveal the following information regarding the privileged communication: (1) the date of the communication; (2) the form of the communication; (3) the identity of all individuals involved in the communication including, where possible, their employer and employment position at the time of the communication; and (4) the general subject matter of the privileged communication.

17. The fees and costs incurred which are reimbursable under the second paragraph of article 14 or under article 26 of the Convention will be borne by:

Apotex, Inc and Apotex, Corp.

Representative: Robert B. Breisblatt, Esq.
Welsh & Katz, Ltd.
120 S. Riverside Plaza • 22nd Floor
Chicago, Illinois 60606-3912
United States of America
Tel. No.: (312) 655-1500
Fax No.: (312) 655-1501

18. Date of Request: _____, 2007

19. Signature and seal of the Requesting authority:

_____
Hon. Sue L. Robinson
United States District Court Judge

20. Attachment:

Questionnaire for Mr. Helmut Hettche (Tab 1)
List of Exhibits for Mr. Helmut Hettche (Tab 2)

Peter D. Dalleo, Clerk of Court

By: _____

Seal of the
United States District Court
for the District of Delaware

787102 / 30234

EXHIBIT 1

Questionnaire For Mr. Helmet Hettche

A. Introduction

Mr. Helmut Hettche is identified as the named inventor on United States Patent No. 5,164,194 ("'194 patent") that issued on November 17, 1992. The '194 patent is entitled: "Azelastine Containing Medicaments." The '194 patent was originally assigned to Asta Pharma AG. The '194 patent is now owned by MedPointe Healthcare, Inc. The '194 patent claims a date of priority based on the filing of a German patent application (P 37 38 681.6) on November 13, 1987. MedPointe has accused Apotex, Inc. and Apotex, Corp. with infringing the '194 patent in seeking approval to market, in the U.S., a generic azelastine nasal spray.

B. General Background Information

1. Will you please state your name and address?

2. When were you born?

3. Please describe your educational background including any degrees obtained?

4. Do you speak English? Can you read and understand English.

5. Please describe your employment history including the dates of employment and the identity of your employers?

6. Between 1983 and 1992, what are the employment positions you held? For each position, please identify your duties and responsibilities as well as the identity of the person or persons to whom you reported.

7. Did you ever work for Asta-Werke AG? If so, when did you work for Asta-Werke AG and what positions did you hold?

8. Was Asta-Werke AG related in any way to Asta Pharma and, if so, what was that relationship if you know?

9. Have you ever been a member of any professional organizations? If so, please identify the professional organizations and your years of membership?

10. Have you authored any articles for publication? If so, please identify the articles that have been published where you are identified as an author?

11. During your employment between 1983 and 1992, did you keep a journal, calendar, lab book, diary or other source for recording your work?

C. Preparation for Judicial Proceeding

1. What, if anything, did you do to prepare for your testimony today?

2. Did you meet with anyone to prepare for your testimony today? Who did you meet with and for how long?

3. Did you review the documents that accompanied the Letters of Request from the United States court in preparation for your testimony today? What other documents, if any, did you review in preparation for your testimony today?

4. Did the documents you reviewed help to refresh your recollection of events surrounding your development of an azelastine nasal spray and azelastine eye drops?

D. Hettche Exhibit 1 – German Priority Document to '194 Patent

1. Please take a look at **Hettche Exhibit 1**? Do you recognize this document? What is this document? Who prepared this document? Why was this document prepared? If you did not prepare this document, what involvement, if any, did you have in its preparation? Does your name appear anywhere in **Hettche Exhibit 1**?

2. Please take a look at **Hettche Exhibit 2** which is a copy of U.S. Patent No.

5,164,194, with a German translation attached. Do you recognize this patent?

3. Are you the sole named inventor on the U.S. '194 patent – **Hettche Exhibit 2**?

4. Looking at **Hettche Exhibit 1** and **Hettche Exhibit 2**, do you understand that there is a relationship between these two exhibits? What is that relationship to the best of your knowledge?

5. Referring to **Hettche Exhibit 1**, please tell us generally what this document is about?

6. Referring to **Hettche Exhibit 2**, please tell us generally what this patent is about?

7. Are the claims of **Hettche Exhibit 1** and **Hettche Exhibit 2** the same? If not, how do they differ?

8. To your knowledge, in what other countries were patents obtained for azelastine containing medicaments where you are the sole named inventor?

E. European Patent No 0 316 633

1. Please take a look at **Hettche Exhibit 3** which is a copy of European Patent 0 316 633. Do you recognize this patent? Are you the sole named inventor on **Hettche Exhibit 3**? Can you please tell us generally what **Hettche Exhibit 3** is about?

2. Looking at **Hettche Exhibit 3** and **Hettche Exhibit 2**, is there any relationship between these two patents and, if so, what is the relationship? Do both of these patents seek patent protection for your development of azelastine containing medicaments?

3. Looking at **Hettche Exhibit 3** and **Hettche Exhibit 1**, is there any

relationship between these two exhibits and, if so, what is the relationship?

4. Please take a look at **Hettche Exhibit 4**, a copy of the decision of the Opposition Division of the European Patent Office mailed on March 28, 1996 with an attached English translation. Do you recognize this document? Who filed an opposition proceeding against your European patent, **Hettche Exhibit 3**? Who is Chemical Pharmaceutical Company, GmbH? At the time, was Chemical Pharmaceutical Company, GmbH a competitor of Asta Pharma AG?

5. Is it correct that the Opposition Division of the European Patent Office revoked your European patent, **Hettche Exhibit 3**? What is your understanding of the reasons that the Opposition Division gave for revoking your European patent, **Hettche Exhibit 3**?

6. Please take a look at **Hettche Exhibit 5**, a copy of the Decision of the Technical Court of Appeals dated April 5, 2000. Do you recognize this document? Is it correct that the Decision of the Technical Court of Appeals affirmed the March 1996 decision of the Opposition Division of the European Patent Office? What is your understanding of the reasons that the Technical Court of Appeals gave for revoking your European patent, **Hettche Exhibit 3**?

7. Is it correct that, as a result of the decisions of the Opposition Branch of the European Patent Office and the Technical Court of Appeals, your European patent, **Hettche Exhibit 3**, is revoked?

8. Please take a look at **Hettche Exhibit 6**, a copy of German Offenlegungsschrift 21 64 058 (with an English translation attached). Do you recognize this patent?

Questionnaire For Mr. Helmet Hettche

9. Looking at **Hettche Exhibit 5**, the decision of the Technical Court of Appeals, please turn to page MPAT0000247, do you see the reference at paragraph II to "DE-C-2 164 058? Do you understand that reference to be the same as **Hettche Exhibit 6**, Offenlegungsschrift 21 64 058?

10. On page 17 of **Hettche Exhibit 5** (MPAT 0000263), the Technical Court of Appeals notices evidence that topical antihistamines are known in the art, and that "considerable amounts of these preparations were still in use." To the best of your knowledge, please identify all topical antihistamine preparations that were known in the art at the time you first conceived of nasal and eye medicaments containing azelastine? Did you consider any of these formulations when arriving at the nasal and eye medicaments containing azelastine?

11. Please take a look at **Hettche Exhibit 7**, a copy of U.S. Patent No. 3,813,384 (with a German translation attached)? Are you familiar with this patent?

12. Referring to **Hettche Exhibit 6**, Offenlegungsschrift 21 64 058, and **Hettche Exhibit 7**, is it your understanding that there is a relationship between these two patents? What is that relationship? Is it correct that **Hettche Exhibit 7** is the U.S. counterpart patent to **Hettche Exhibit 6**?

13. Referring to **Hettche Exhibit 5**, what role, if any, did you play in the opposition proceedings that resulted in the April 5, 2000 decision of the Technical Court of Appeals of the European Patent Office?

14. Looking at **Hettche Exhibit 5** at paragraph III under the heading"Facts and Claims" (MPAT0000247-248), could you please describe what the list of publications represents?

Questionnaire For Mr. Helmet Hettche

F. Azelastine

1. Please describe all of the work you have done with azelastine? In what forms, i.e. sprays, tablets, ointments, etc. have you worked with azelastine? Please identify, in order, the forms of azelastine you worked with and when.

2. During what period of time in your employment history did you work with azelastine?

3. Generally, please describe the various symptoms, illnesses or conditions that you were aware of that are treatable with azelastine? When did you first know that azelastine could be used to treat the symptoms, illnesses or conditions that you just described?

4. When did you first know of the anti-allergic and anti-histamine properties of azelastine?

5. **Hettche Exhibit 6** is a copy of German Patent No. 21 64 058 Have you seen this German '058 patent before?

6. When did you first became aware of the existence of **Hettche Exhibit 6**?

7. Please describe the circumstances under which you first became aware of the German '058 patent.

8. At the time you became aware of the existence of **Hettche Exhibit 6**, the German '058 patent, did you read it? When do you recall first reading **Hettche Exhibit 6**, the German '058 patent? When was the last time you recall reading **Hettche Exhibit 6**?

9. Looking at **Hettche Exhibit 1**, the German '681 patent, on page 5 (MP0034), do you see where the German '681 patent is cited?

10. In the German '681 patent application, it is stated that the German '058 patent disclosed the anti-allergic and antihistimine properties of azelastine, correct?

11. Looking at **Hettche Exhibit 2**, the German '058 patent is cited as disclosing the anti-allergic and antihistimine properties of azelastine at Col. 1, lines 29-31, correct?

12. Looking at **Hettche Exhibit 6**, do you agree that this patent discloses the anti-allergic and anti-histamine properties of azelastine?

13. Please describe generally how you got involved in developing a nasal spray containing azelastine?

14. With regard to a nasal spray containing azelastine, what symptoms, illnesses or conditions were you trying to treat with a nasal spray?

15. Please describe generally how you got involved in developing azelastine eye drops?

16. With regard to azelastine eye drops, what symptoms, illnesses or conditions were you trying to treat with a eye drops?

17. What research into papers, publications, treatises, reference materials and patents did you conduct in connection with the development of an azelastine nasal spray.

G. Inventorship

1. When did you begin to work on an azelastine nasal spray?

2. When did you begin to work on azelastine eye drops?

3. **Hettche Exhibit 8** is a December 1982 Asta-Werke AG Toxicology Report. Are you familiar with this report? When did you first become aware of this report? Did you have any involvement in the study underlying this report? Do you have

any understanding as to why Asta-Werke AG conducted the underlying study and prepared the Toxicology Report?

4. At the time of the Asta-Werke AG Toxicology Report, were you working at Asta-Werke, AG?

5. Referring to page ATI00001105 of **Hettche Exhibit 8**, please review the first full paragraph. Could you please describe your understanding of the substance of this first paragraph.

6. What involvement, if any, did you have in the formulation of 0.1% azelastine solution to be applied to the eyes of guinea pigs as described in the first paragraph on page ATI00001105? What is meant by the statement that A 5610 acts like most antihistamines?

7. Were you aware that your employer, Asta-Werke AG, in the 1982 time-frame was conducting studies of azelastine solutions for application to the eyes of guinea pigs? If so, how did you know about this study?

8. Please review Abstract 76 in **Hettche Exhibit 9**, referring to an article by Dr. Chand and others involving the effect of aerosolized azelastine on guinea pigs published in 1985 in Pharmacologist. Having reviewed Abstract 76, do you understand that Dr. Chand describes a 1% aerosolized solution of azelastine? Do you also understand that Dr. Chand reports that a 1% aerosolized solution of azelastine administered to guinea pigs had a prophylactic effect before an allergen challenge?

9. Did you have any involvement in the study conducted by Dr. Chand as reported in **Hettche Exhibit 9**? If so, what was your involvement? Did you suggest or participate in the selection of a 1% aerosolized solution for use in the study conducted by

Dr. Chand?

10. Prior to 1985, please describe other tests and studies you were aware of involving azelastine solutions and your participation, if any, in these tests or studies?

11. Please describe the circumstances that led you to begin work on the development of an azelastine nasal spray and eye medicaments? Which came first, the development of an azelastine nasal spray or an azelastine eye medicament? Whose idea was it to use the azelastine solution as a nasal and eye medicament?

12. Please identify who, if anyone, you worked with in developing an azelastine nasal spray?

13. At the time you began to work on azelastine nasal and eye medicaments, what other nasal and eye medicaments were you aware of? What were the ingredients that were used in other nasal and eye medicaments and what symptoms, illnesses or conditions were they used to treat?

14. At the time you began to work on azelastine nasal and eye medicaments, what other nasal and eye medicaments were you aware of that contained antihistamines?

15. What, if anything, did you know about azelastine that led you to believe it should be used in nasal and eye medicaments?

H. Timing Of Development Of Azelastine Nasal Spray

1. When did you first produce an azelastine nasal spray?

2. What was the concentration of the first azelastine nasal spray you developed?

3. What concentrations did you consider in formulating your first azelastine nasal spray? How did you decide on those concentrations?

Questionnaire For Mr. Helmet Hettche

4. Referring to **Hettche Exhibit 2**, your U.S. '194 patent, please review Col. 2, lines 35 through 47. You have identified water as the preferred solvent for the azelastine nasal spray and eye drops, is that correct? Is it also your understanding that your U.S. '194 patent, **Hettche Exhibit 2**, states that azelastine nasal drops and sprays, "preferably" contain preservatives and stabilizers, but that nasal drops and sprays can be formulated without preservatives and stabilizers?

5. What preservatives or other excipients did you include in the first azelastine nasal spray you developed that included preservatives and excipients? At the time you included preservatives and excipients in your azelastine formulation, were you aware of other nasal or eye medicaments using those preservatives and/or excipeints? How did you decide on the specific preservatives and excipients you used in your azelastine nasal formulation?

6. What was the concentration of the preservatives or other excipients you included in the first azelastine nasal spray? Were you aware of other nasal or eye medicaments using those same preservatives and/or excipients that you selected?

7. Please take a look at **Hettche Exhibit 10** (AS-MEDA0001568), a document produced by MedPointe from the files of Asta-Meda? Do you recognize this document? Do you recognize that this document was produced from a folder that bears your handwriting? Did you draw the box around the text for "Beispiel 24" on this document? Why did you do so? Were you aware of Beispiel 24 at the time you suggested producing nasal and/or eye medicaments containing azelastine?

8. What would be the percent (weight/weight) of azelastine contained in a medicament produced by dissolving 0.3g of azelastine in 100ml of sterilized water?

Would this percent concentration fall within the range of claim 2 of **Hettche Exhibit 2**, the '194 patent? Would this percent concentration fall within the range of claim 3 of **Hettche Exhibit 2**, the '194 patent? Would this percent concentration fall within the range of claim 4 of **Hettche Exhibit 2**, the '194 patent?

9. If a medicament was produced according to Beispiel 24 in **Hettche Exhibit 10** using azelastine as disclosed in **Hettche Exhibit 6**, would that formulation fall within the range of claims 2, 3 and 4 of **Hettche Exhibit 2**? Would the formulation be an aqueous solution?

I. Hettche Exhibit 11

1. Please take a look at **Hettche Exhibit 11** (AS-MEDA0000601-602). Do you recognize this document?

2. Did you receive a copy of this document on or around September 6, 1985? Does the reference in the "Cc" to "Dr. He" refer to you?

3. At the time of **Hettche Exhibit 11**, what was Dr. Aurich's employment position? What was Prof. Dr. Breuel's employment position?

4. How did Dr. Aurich become aware that you produced an A 5610 nasal spray?

5. Is there any significance to the identification of the azelastine nasal spray as "A 5610"? Was there a classification system for identifying samples of azelastine nasal spray. What does the "A" denote, if anything? What does the number "5610" denote, if anything?

6. When did you first produce the A 5610 nasal spray referenced in **Hettche Exhibit 11**?

Questionnaire For Mr. Helmet Hettche

7. Was the nasal spray identified in **Hettche Exhibit 11** the first azelastine nasal spray you developed? If not, please describe the formulation and ingredients of other azelastine nasal sprays you developed before the A 5610 nasal spray referenced in **Hettche Exhibit 11**. How were these earlier azelastine nasal spray formulations identified?

8. How did you arrive at the formulation using 0.1% solution of azelastine.?

9. What preservatives or other excipients did you use in the nasal spray referenced in **Hettche Exhibit 11** ? What was the concentration of the preservatives or other excipients used in A 5610? How did you determine the concentrations?

10. Who was Dr. Molliere? What was his employment position at the time? How did Dr. Molliere's employment position compare to yours?

11. What role did Dr. Molliere play in the development of the nasal and eye medicaments containing azelastine? What role did Dr. Molliere play in the development of the azelastine nasal spray formulation referenced in **Hettche Exhibit 11**?

12. What was the exact formulation of the azelastine nasal spray self-administered by Dr. Molliere and you including any preservatives, stabilizers or other excipients or impurities? Was there any difference between the nasal spray formulations tested by you and tested by Dr. Molliere? If so, what was the exact formulation of the azelastine nasal spray self-administered by Dr. Molliere, including any preservatives, excipients of impurities?

13. Did you conduct any testing before you and Dr. Molliere personally used the A 5610 nasal spray?

14. Did you conduct any testing in determining the concentration levels used

in A 5610?

15. What prompted you to select azelastine?

16. At the time of **Hettche Exhibit 11**, were you working on the development plan for Azelastine in tablet form as referenced by Dr. Aurich? If so, what was your role?

17. In **Hettche Exhibit 11**, on the second page, Dr. Aurich refers to Hismanal (astemizole). Did you know about this product at the time? What was this product? Who introduced it in Germany? Was Hismanal a nasal spray? Did you know the formulation of Hismanal?

18. Was your work on the formulation of an azelastine nasal spray approved, in advance, by your superiors?

19. Dr. Aurich writes in **Hettche Exhibit 11** that Dr. Muckenschnabel suggested there would be no problem producing solutions that were half and twice the dosage of the 0.1% solution you produced. Prior to Sep. 6, 1985, did you suggest to Dr. Muckenschnabel that he produce azelastine solutions that were half and twice the dosage of the 0.1% solution you produced?

20. Dr. Aurich also writes that "with this dosage it can be assumed that respective studies regarding fitness to drive will not produce any evidence of drowsiness." Do you agree with this statement? Why?

21. Dr. Aurich also suggests supplementing development to include "simultaneously such nasal spray as well as eye drops." Is it true that Dr. Aurich was the first to suggest using the azelastine solution as an eye drop? If not, who suggested to Dr. Aurich that the azelastine solution could be used as an eye drop and when?

22. Did Dr. Molliere and you self-administer any azelastine eye drop formulations prior to September 6, 1985. If so, please identify the exact formulation of the azelastine eye drop formulation and when it was self-administered by Dr. Molliere and you?

23. Before September 6, 1985, please identify any studies conducted by you or under your direction concerning the application of an azelastine solution directly to the eye?

J. Hettche Exhibit 12

1. Please take a look at **Hettche Exhibit 12** produced by Asta-Meda as AS-MEDA0004168-4169. Do you recognize this document? Did you prepare this document?

2. What is meant by the title "Notice to Dr. Herbst?"

3. On the first page, under Azelastine nasal spray is a reference to "PEGF-Dr. He/Jg of 9/30/1985" What does this refer to? Who does "Dr. He" refer to? Who does "Jg" refer to? What does PEGF refer to? Please describe this Notice of September 30, 1985? Why did you prepare this notice and who was it directed to?

4. In your first sentence, you write: "Corresponding to the above-named notice and a decision of the research coordinate on 10/17/85, the development of Azelastine nasal spray has started at 0.05%, 0.1%, and 0.2% Azelastine hydrochloride." What are you referring to when you refer to the "above-named notice." What does the 'research coordinate" refer to? Were the 0.05%, 0.1%, and 0.2% solutions developed in response to Dr. Muckenschnabel's suggestions that they could easily be formulated? Who produced these solutions? Did Dr. Muckenschnabel direct the persons producing

these solutions?

5. At the bottom of page 1 and the top of page 2 of **Hettche Exhibit 12**, you describe the 0.2% solution produced at the suggestion of Dr. Muckenschnabel. Who was responsible for choosing the preservatives and excipients described in **Hettche Exhibit 12**? Was this the first time preservatives and excipients were used in solutions containing azelastine?

6. In the last sentence on page 2 of **Hettche Exhibit 12**, you indicate that the 0.2% solution "was released for animal experimentation with AN 76 0001 of 1/23/86." What does AN 76 0001 refer to? The 0.2% solution was released for animal experimentation after Dr. Molliere and you had self-administered a 0.1% azelastine solution, correct?

K. Hettche Exhibit 13

1. Please take a look at **Hettche Exhibit 13**. Did you prepare this document on or about August 13, 1990? In the first paragraph, you indicate Carter Wallace suggested adjusting the pH of the nasal formulation. Who made the suggestion at Carter Wallace? What role did Carter Wallace play in formulating nasal and eye formulations containing azelastine?

L. Hettche Exhibit 14

1. Please take a look at **Hettche Exhibit 14** (AS-MEDA0001938). Do you recognize this document? It this document in your handwriting?

2. What is the date of **Hettche Exhibit 14**?

3. What prompted you to prepare this note?

4. What is this note about?

Questionnaire For Mr. Helmet Hettche

5. Does the reference to "nasal spray" refer to a nasal spray containing azelsastine?

6. Was this the first time you determined that an azelastine nasal spray had positive results for treating a regular cold? What do you mean by "positive results"? How did you measure the results?

7. How did the azelastine nasal spray referenced in **Hettche Exhibit 14** compare to A 5610 referenced in **Hettche Exhibit 11**? What were the similarities? What were the differences?

8. As of February 18, 1986, had a three month stability trial been conducted as mentioned by Dr. Aurich in **Hettche Exhibit 11** ? If so, what was the result of the stability trial? What is a stability trial?

9. As of February 18, 1986, had a local compatibility trial been conducted as mentioned by Dr. Aurich in **Hettche Exhibit 11**? What is meant by a local compatibility trial?

10. What were the results of the local compatibility trial?

M. Hettche Exhibit 15

1. Please take a look at **Hettche Exhibit 15 (AS-MEDA0000600)**. Do you recognize this document? Generally, what is this document?

2. What is the date of **Hettche Exhibit 15**?

3. Who is Dr. Ulbrich and what was his position at the time you prepared this document?

4. Why did you prepare this document?

5. What do you mean when you write that "the tests currently performed deal

with a clarification of the effectiveness of Azelastine nasal spray for seasonal rhinitis?"

6. You refer to your own experience with the effectiveness of the nasal spray during a common cold. Is this referring back to experience that is reported in **Hettche Exhibit 14** (AS-MEDA0001938)?

7. In August 1987, what changes, if any, were made to the formulation of an azelastine nasal spray as compared to the formulation of A 5610 as identified by Dr. Aurich in **Hettche Exhibit 11**?

8. Between September 1985 and August 1987, can you describe the various formulations of an azelastine nasal spray that were prepared and tested?

9. Did the planned clinical trial 2611 take place? If so, please describe the clinical trial. When did it take place and what was the result?

N. Hettche Exhibit 16

1. Please take a look at **Hettche Exhibit 16**, a copy of U.S. Patent No. 4,704,387 and the German translation. Do you recognize this U.S. patent claiming substituted benzylphthalazinones having antiallergic and antihistamine action? Please review Column 8, lines 21-26. Is it your understanding that solutions for application to the skin and mucous membrane are discussed? Is it also your understanding that the claimed percentage concentration of active materials are in the range of 0.1% to 3% of active ingrediaents with respect to solutions? Does this range fall within or encompass the range claimed in claims 2, 3 and 4 of your '194 patent, **Hettche Exhibit 2**?

2. At Column 7, lines 58-61 of **Hettche Exhibit 16**, the specification states that the antiallergic action of the claimed compounds is comparable to the known medicine azelastine. What is the relationship between the claimed compounds in

Hettche Exhibit 16 and azelastine?

3. Did you review **Hettche Exhibit 16** prior to formulating nasal and eye medicaments containing azelastine? Knowing the derivatives of azelastine could be administered directly to the mucous membranes, would you have expected that azelastine could also be administered in that manner? Given the antiallergic action of azelastine was comparable to the compounds claimed in **Hettche Exhibit 16**, would you have expected the concentration of azelastine solutions for topical application to the mucous membranes to be effective in similar concentrations disclosed in **Hettche Exhibit 16**?

O. Self-Administration Of Azelastine

1. Is it correct that you self-administered an azelastine nasal spray to treat both your hay-fever and a regular cold? What made you decide to formulate an Azelastine nasal spray?

2. Back in 1985, if you were not inclined to conduct self-administration of an azelastine nasal spray for your hay-fever and colds, what were the other testing methods available to determine whether azelastine, in a nasal spray, would work? Please describe the various testing methods that could have been used.

3. What was it about azelastine that compelled you to use the formulation on yourself?

4. How did you know that you could use the azelastine nasal spray formulation on yourself without any adverse health consequences? Please describe what you knew at the time about azelastine or nasal sprays or similar formulations in general that led you to conclude that self-administration of an azelastine nasal spray would not hurt you?

5. How did the concentration of azelastine in the nasal spray compare to the azelastine concentration undergoing development in a tablet form at the time?

6. What side-effects, if any, did you encounter in the self-administration of the azelastine nasal spray?

7. What side effects, if any, did Dr. Molliere encounter in the self-administration of the azelastine nasal spray?

8. Do you know what prompted Dr. Molliere to join you in the self-administration of the azelastine nasal spray?

9. Did Dr. Molliere ever express any reservations about potential adverse consequences of self-administering the azelastine nasal spray and, if so, what convinced him to proceed with self-administration?

10. Prior to your self-administration of an azelastine nasal spray, did you have an expectation that it would work? If so, why did you expect it to work?

P. Hettche Exhibit 17

1. **Hettche Exhibit 17** is a copy of German Patent Application No. 35 39 873. Have you seen this German '873 application before?

2. When do you recall the first time you became aware of the existence of the German '873 application?

3. Please describe the circumstances that led to your awareness of the German '873 application.

4. At the time you became aware of the existence of **Hettche Exhibit 17**, the German '873 application, did you read it? When do you recall first reading **Hettche Exhibit 17**, the German '873 application?

Questionnaire For Mr. Helmet Hettche

Q. Hettche Exhibit 18 - German Patent No. 3,433,776

1. **Hettche Exhibit 18** is a copy of German Patent No. 3,433,776 identifying Dr. Jurgen Engel and Gerhard Scheffler as the named inventors. Have you seen this German '776 patent before?

2. When do you recall the first time you became aware of the existence of the German '776 patent?

3. Please describe the circumstances that led to your awareness of the German '776 patent.

4. At the time you became aware of the existence of **Hettche Exhibit 18**, the German '776 patent, did you read it? When do you recall first reading **Hettche Exhibit 18**, the German '776 patent?

5. When did you become aware that Dr. Engel had filed a patent on derivatives of azelastine?

6. Did you consult or work with Dr. Engel in deciding what concentrations of azelastine would be favorable in a nasal spray?

R. Hettche Exhibit 19

1. Please refer to **Hettche Exhibit 19** (AS-MEDA0000617-629), a copy of a document, entitled "Vademecum" produced from the files of Asta-Meda. Are you familiar with this reference? Do you agree that this reference teaches external and internal administration of medicinal drops? In the case of the external administration of medicinal drops, do you understand this reference to teach the application of medicinal drops to the eyes and to the nose? In the case of the external administration of drops to the nose, do you understand this reference to teach applying drops to the nose using a

spraying mechanism? In the case of external administration of nasal drops, do you understand this reference to teach that many nasal drops also find application as eye drops?

S. Hettche Exhibit 20

1. Please take a look at **Hettche Exhibit 20**, a March 1971 article. Are you familiar with this article? How and when did you first become aware of this article? In 1971, was it common to administer medicaments to the nose in drops to treat conditions of the nasal mucosa associated with colds or allergies? Are you familiar with the term nasentropfen? When did you first hear the term nasentropfen. Could you please explain what this term means to you.

2. Please review Table 2 in **Hettche Exhibit 20**. Is it your understanding that Table 2 identifies nasal drops available in the market at the time of this article? Is it also your understanding that Table 2 identifies the following nasal drops containing antihistimines: (i) Antisin-Privin; (ii) Aqua-Mistol; (iii) Biomydrine; (iv) nasoptol spray; (v) Bebdosator; (vi) Tecoryl; and (vii) vibrocil?

3. Table 2 discloses Antisin-Privin as a nasal drop available in the market. To the best of you knowledge, does this medicament contain the same active ingredients used in eye drops?

4. The last sentence on page 2 and the top of page 3 of **Hettche Exhibit 20** states: "The frequent local use of antihistamines on the nasal mucosa, according to current experimental results, leaves little to be expected, aside from a slight anesthetic effect of certain antihistamines." Were you aware of this information at the time you produced the first nasal medicament containing azelastine?

T. Hettche Exhibit 21

1. Please take a look at **Hettche Exhibit 21**, an Antistin-Privin package insert. Are you familiar with this package insert for Antistin-Privin eye drops? Are you familiar with this medicament? What symptoms, illnesses or conditions does this medicament treat? Is the concentration of antazoline sulphate in Antistin-Privin similar to the concentrations for azelastine found in claims 2, 3 and 4 of your '194 patent, **Hettche Exhibit 2**? Is the concentration of benzalkonium chloride within the range found in claim 8 of your '194 patent, **Hettche Exhibit 2**? To the best of your knowledge, what is the purpose of the 0.002% m/v benzalkonium chloride used in Anistin-Privin?

U. Hettche Exhibit 22

1. Please take a look at **Hettche Exhibit 22**, produced by Asta-Meda as AS-MEDA0007755. Do you recognize this reference document produced by MedPointe from the Asta-Meda files and referring to medications for use in the eye, ear and nose? What reference source do you recognize this page as coming from?

2. Please take a look at the section of **Hettche Exhibit 22** designated as 7.3.1 entitled "Nasal drops." To the best of your knowledge, what concentrations of benzalkonium chloride are disclosed in Table 5.96? This reference shows the use of benzalkonium chloride as a preservative in eye drops, correct?

V. Hettche Exhibit 23

1. Please take a look at **Hettche Exhibit 23** which is a copy of an article entitled "The effects of nasal drops on the ciliary beat frequency of chicken embryo tracheas." Were you aware of this 1981 article from the journal Rhinology examining the effects of nasal drops on the ciliary beat frequency after its publication? How and when

do you recall first learning of this journal article?

2. Could you please review Table H. How many of the nasal drops in Table H contain benzalkonium chloride in the percentage concentrations disclosed in claims 5 and 8 of your U.S. '194 patent, **Hettche Exhibit 2**?

3. Please review Table III. How many of the nasal formulations identified in Table III contain thimerosal or benzalkonium chloride in the concentration ranges disclosed in claims 5 and 8 of your U.S. '194 patent, **Hettche Exhibit 2**?

4. At the page numbered as AS-MEDA0000332, Figure 6 is said to demonstrate "the effects of preparations containing drugs which are used against allergic diseases and sometimes against vasomotor rhinitis." Reviewing Figure 6, how many of these nasal drop medicaments contain antihistamines? Could you please identify any other antihistamine containing nasal drops that are not mentioned in Figure 6.

5. At the last page of **Hettche Exhibit 23**, it is stated that it is unlikely that systemic administration of the drugs discussed in the reference will be preferable to local administration. Do you agree with this statement?

X. Hettche Exhibit 24

1. Please take a look at the article that has been marked as **Hettche Exhibit 24**. Are you familiar with **Hettche Exhibit 24**? How and when did you become aware of the publication of this article? Do you have any clinical experience with nasal drops or eye drops prior to your work on nasal sprays containing azelastine? What do you understand this article to show with respect to U.S. literature discouraging local application of antihistamines?

Questionnaire For Mr. Helmet Hettche

Y. Hettche Exhibit 25

1. Directing your attention to **(Hettche Exhibit 25)** (AS-MEDA0003522-3525), that is your signature on the front page of **Hettche Exhibit 25**, correct?

2. You recognize Dr. Engel's signature which is also on the front page of **Hettche Exhibit 25,** correct?

3. Hettche **Exhibit 25** is a report dated September 13, 1988, correct?

4. The title of **Hettche Exhibit 25** is development pharmaceutics of Azelastine Hydrochloride 0.1% nasal spray, correct?

5. The study was conducted at ASTA Pharma AG, correct?

6. You were the study director, correct?

7. Hettche **Exhibit 25** is the report of the study conducted at ASTA Pharma **AG?**

8. You were the author of the report marked Hettche **Exhibit 25**, correct?

9. Dr. Engel reviewed and approved the report, didn't he?

10. Please review the first heading, titled "Preservatives" on Page 2 of **Hettche Exhibit 25.**

11. You represent in **Hettche Exhibit 11** that your reasons for choosing benzalkonium chloride as the preservative in the nasal spray formulation was based on information contained in the scientific literature, correct?

12. The literature you consulted with regard to the preservatives and presertive concentrations to use in the nasal medicament are listed on the final page of **Hettche Exhibit 25**, correct?

13. The literature you consulted and which is referenced on the final page

suggests benzalkonium chloride as a preservative, correct?

14. To the best of your knowledge, have any other nasal medicaments used benzalkonium chloride as a preservative in the concentrations you selected based on the literature?

15. Please review the remainder of the report marked **Hettche Exhibit 25.**

16. It's fair to say that you represent in this report that the nasal medicament you formulated was justified based on the literature and that you followed the literature when you formulated the nasal medicament with respect to preservatives, tonicity, pH, buffers, and thickening agents?

17. You would agree that one skilled in the art wishing to administrer a medicament in drops to the nasal musosa would be able to formulate such a medicament by consulting the references you relied on in formulating the azelastine medicine?

18. The literature you consulted also suggested the concentration of benzalkonium chloride for nasal medicaments, correct?

Z. Azelastine Eye Drops

1. Please describe what involvement, if any, you had in the development of azelastine eye drops?

2. Who else was involved in the development of azelastine eye drops?

3. When was the first azelastine eye drops developed? How was it developed?

4. Who had the idea to develop an azelastine eye drop?

5. How did the first formulation of an azelstine eye drop compare to the formulation of the azelastine nasal spray? Were the formulations the same of did they

differ and, if so, how did they differ?

6. Did you or anyone else engage in self-administration of azelastine eye drops as you did with the azelsatine nasal spray?

7. Did the first formulation of an azelastine eye drop have the same concentration level of azelastine as found in the A 5610 nasal spray?

AA. Lawrence Hymo

1. Do you know a U.S. patent attorney by the name of Lawrence Hymo? If so, how do you know Mr. Hymo?

2. Have you ever met Mr. Hymo in person and, if so, please generally describe the circumstances where you have met Mr. Hymo in person.

3. When was the last time you had any contact with Mr. Hymo? What were the circumstances that last brought you into contact with Mr. Hymo?

BB. Dr. Istvan Szelenyi

1. Do you know Dr. Istvan Szelenyi and, if so, please describe how you know Dr. Szelenyi?

2. When did you first have any contact with Dr. Szelenyi?

3. Have you ever worked with or collaborated with Dr. Szelenyi and, if so, please describe the work or collaboration that you have had with Dr. Szelenyi?

CC. Hettche Exhibit 26

1. Please take a look at **Hettche Exhibit 26**, entitled "Declaration Under 37 CFR 1.132," a German translation is attached. Do you recognize this document? What is this document?

2. Do you recognize the signature on the last page of **Hettche Exhibit 26**?

Questionnaire For Mr. Helmet Hettche

DD. Hettche Exhibit 27

1. Please take a look at **Hettche Exhibit 27**, entitled "Inhibition of allergic histamine release from rat peritoneal mast cells." Do you recognize this document? Where are rat peritoneal mast cells located?

2. Who prepared this document?

3. Is this the materials and methods used by Dr. Szelenyi that are referenced in his January 23, 1990 Declaration?

4. At the time of his January 1990 Declaration, where did Dr. Szelenyi work?

5. What was Dr. Szelenyi's educational background, if you know.

6. Why was Dr. Szelenyi approached to conduct this experiment?

7. What role, if any, did you play in the selection of Dr. Szelenyi to conduct the experiment described in **Hettche Exhibits 26 & 27**?

8. What role did you play in designing the comparison experiment Dr. Szelenyi conducted?

9. Had you worked with Dr. Szelenyi before he conducted the comparison experiment described in **Hettche Exhibit 27**? If so, please describe the work you have previously done with Dr. Szelenyi.

10. What was the goal of the comparison experiment to be conducted by Dr. Szelenyi?

11. Why was it necessary to employ Dr. Szelenyi to conduct the experiment described in **Hettche Exhibit 27**?

12. Looking at **Hettche Exhibit 26**, paragraph 1, where it recites "Experiments have been conducted under my supervision to determine the effects of

compounds disclosed in the above-referenced application and the cited U.S. Patent 4,704,387." What compounds disclosed in your pending patent application did Dr. Szelenyi test?

13. Who provided or prepared the compounds to be used by Dr. Szelenyi in the experiment?

14. What was given to Dr. Szelenyi so that he could declare that his experiment could determine the effects of the compounds disclosed in the above-referenced application? Please describe what was given to him and by whom? What language was he given this material in?

15. What was given to Dr. Szelenyi so that he could determine the compounds disclosed in U.S. Patent No. 4,704,387? Please describe what was given to him and by whom? What language was he given this material in?

16. Please disclose the formulations of azelastine from your pending U.S. patent application that Dr. Szelenyi tested according to the procedures in **Hettche Exhibit 27**?

17. Please disclose the compounds from the Engel '387 patent that Dr. Szelenyi tested according to the procedures in **Hettche Exhibit 27**?

18. If Dr. Szelenyi did not test any other compounds from the Engel '387 patent other than Example 1, why did he restrict his experiments to only a comparison with Example1?

19. What role did you play in the selection of the compounds from the Engel '387 patent that Dr. Szelenyi should compare to your azelastine formulation?

20. Did Dr. Szelenyi test, for comparison purposes, the compound in Example

1 of the Engel '387 patent (of Example 1 in the German counterpart)?

21. According to Dr. Szelenyi, the compound he tested from the disclosure in your patent application was twice as effective as the compound in Example 1 of the Engel '387 patent, as disclosed in paragraph 5 of his January 1990 Declaration, **Hettche Exhibit 26**, correct?

22. What was the formulation of the azelastine compound Dr. Szelenyi compared to Exhibit 1? Who prepared the azelastine formulation for the comparison test?

23. If you are unable to recall the azelastine formulation used by Dr. Szelenyi, how would you go about trying to find this information today?

24. Did you receive any type of communication from Dr. Szelenyi regarding the results of his experiments? If so, what did you receive?

25. Did Dr. Szelenyi compare your azelastine compound to the compound disclosed in Example 2 of the Engel '387 patent? If so, what was the result of a comparison of the effectiveness of your azelastine compound with the effectiveness of the compound in Example 2? If not, why didn't Dr. Szelenyi compare the effectiveness of your azelastine compound to Example 2?

26. Who made the decision not to test your azelastine compound against the compound in Example 2 of the Engel '387 patent?

27. Did Dr. Szelenyi compare your azelastine compound to the compound disclosed in Example 3 of the Engel '387 patent? If so, what was the result of a comparison of the effectiveness of your azelastine compound with the effectiveness of the compound disclosed in Example 3? If not, why didn't Dr. Szelenyi compare the

effectiveness of your azelastine compound to Example 3?

28. Who made the decision not to test your azelastine compound against the compound in Example 3 of the Engel '387 patent?

29. Did Dr. Szelenyi compare your azelastine compound to the compound disclosed in Example 4 of the Engel '387 patent? If so, what was the result of the comparison of the effectiveness of your azelastine compound with the effectiveness of the compound disclosed in Example 4? If not, why didn't Dr. Szelenyi compare the effectiveness of your azelastine compound to Example 4?

30. Who made the decision not to test your azelastine compound against the compound in Example 4 of the Engel '387 patent?

31. Did Dr. Szelenyi prepare a report of the results from his comparisons of your azelastine compound with compounds disclosed in the Engel '387 patent?

32. Did you review Dr. Szelenyi's January 1990 Declaration before it was submitted to the U.S. Patent Office?

33. What role did you play in Dr. Szelenyi's experiment?

34. Did you provide Dr. Szelenyi with the azelastine compound he used in his experiment?

35. Who prepared the compounds based on the disclosure in the Engel '387 patent used by Dr. Szelenyi in his comparison experiment?

36. Was Dr. Szelenyi paid for performing the comparison experiment and, if so, by whom was he paid?

Questionnaire For Mr. Helmet Hettche

EE. Hettche Exhibit 28

1. Please take a look at **Hettche Exhibit 28**. Do you recognize this document? What is it?

2. Do you recognize the signature on page 2? Who signed it? Is this the same Dr. Szelenyi that signed the previous Declaration, **Hettche Exhibit 26**?

3. Do you understand that this Declaration was also submitted to the U.S. Patent Office in connection with your patent application that led to issuance of the '194 patent?

4. Why was it necessary to obtain a second declaration from Dr. Selenyi?

5. Did Dr. Szelenyi conduct additional experiments or comparisons in connection with his second Declaration? If so, please describe the additional experiments or comparisons he conducted.

6. Looking at paragraph 1 of **Hettche Exhibit 28**, it states: "I further declare and state that, in the experiments described in my previous declaration, the same amounts of the respective medicines were used, i.e., azelastine and the compound disclosed in Example 1 of U.S. Patent 4,704,387." Does this confirm that Dr. Szelenyi only conducted a comparison of your azelastine compound with the compound disclosed in Example 1 of the Engel '387 patent?

7. Did you review this Declaration before it was submitted to the U.S. Patent Office?

8. What involvement did you have in the preparation of Dr. Szelenyi's Second Declaration?

9. In paragraph 2 of the Declaration, Dr. Szelenyi refers to "the nasal cavity

contained about 2.5 ml mucus." What nasal cavity is he referring to in his experiment?

10. Isn't it correct that bathing rat peritoneal mast cells in an azelastine solution in a test tube does not involve applying azelastine to the "nasal cavities?" Would you agree that Dr. Szelenyi's second declaration does not involve the same study disclosed in his first declaration? Would you agree the second declaration misrepresents the studies conducted in the first declaration? Would you further agree that the second declaration does not clarify or further describe the experiments described in the first declaration? What study was Dr. Szelenyi referring to that involved applying azelastine to the "nasal cavity contain[ing] about 2.5 ml mucus?"

FF. Other Contact With Dr. Szelenyi

1. Did you have any other contact with Dr. Szelenyi during the prosecution of your U.S. patent application?

2. In March 1991, do you recall that you sent Dr. Szelenyi a letter and memorandum concerning the U.S. Patent Application? If so, what was the memorandum you recall sending him and what did you say in it?

3. Do you recall that Dr. Szelenyi prepared and sent you a memorandum or a report in April 1991 regarding the U.S. Patent Application?

4. When was the last time you spoke with Dr. Szelenyi? What were the circumstances that brought about your last contact with Dr. Szelenyi?

Questionnaire For Mr. Helmet Hettche

GG. Dr. Gerhard Scheffler

1. Did you know Dr. Gerhard Scheffler? If so, how do you know Dr. Scheffler?

2. Did you ever work for or with Dr. Scheffler? If so, please describe the work you have done with Dr. Scheffler and the time frame in which the work was performed.

HH. Dietrich Vogelsang

1. Did you ever know Dietrich Vogelsang? If so, how did you know Mr. Vogelsang?

2. Did you ever work for or with Dietrich Vogelsang? If so, please describe the work you have done with Dietrich Vogelsang.

II. Dr. Juergen Engel

1. How do you know Dr. Juergen Engel?

2. Between 1985 and 1992, did your duties and responsibilities bring you into contact with Dr. Engel. If so, please describe the interactions you had with Dr. Engel during this time frame?

3. Between 1985 and 1992, what employment positions did Dr. Engel hold and how did his employment positions relate, if at all, to the employment positions you held during this same time period?

4. Did you consult with Dr. Engel in connection with your work on an azelastine nasal spray? If so, what did you discuss with Dr. Engel about an azelastine nasal spray?

5. Were you aware of Dr. Engel's work with azelastine before you began

working on a nasal azelastine spray? What did you know about Dr. Engel's work before you started working on an azelastine nasal spray?

JJ. Dr. Naresh Chand

1. Do you know Dr. Naresh Chand? How do you know Dr. Chand?

2. Did you have any communications or contact with Dr. Chand at the time you were developing an azelastine nasal spray? If so, what was the nature of your communications? Did you have access to Dr. Chand's protocols, lab notebooks and/or research reports?

3. What other scientists or employees at Carter-Wallace did you work with to formulate Azelastine medicines? What were their names? What other Azelastine medicines did you work on with them? What methods of administration of Azelastine medicines did you work on with them? In what years did you work on formulations and methods of administration of Azelastine medicines with other scientists and/or physicians employed by Carter Wallace?

4. At the time of your communications with Dr. Chand, who was his employer and what was his position?

5. What brought you into contact with Dr. Chand?

6. Were you aware of Dr. Chand's work with azelastine before you began work on an azelastine nasal spray? If so, what did you know about Dr. Chand's work with azelastine?

7. Did you work, consult, or collaborate with scientists in Japan, Australia, Ireland or any other country with respect to azelastine containing medicaments?

Questionnaire For Mr. Helmet Hettche

KK. Reading Material

1. In the 1980 - 1992 time frame, did you subscribe to any scholarly or scientific journals or papers? If so, please name the journals or papers to which you subscribed?

2. In the 1980 - 1992 time frame, did Asta Medica AG subscribe to scholarly or scientific journals or papers that were routed to you for review?

3. In the 1980 - 1992 time frame, did you have access to a scientific library for research? If so, what library?

4. In the 1980 - 1992 time frame, did you keep a collection of books in your office or work space? If so, what were some of the titles of the books you had in your office or work space?

5. In the 1980 - 1992, please identify the reference books or treatises that you may have consulted on a regular basis in connection with your work?

LL. Preservatives

1. In 1985, were you aware that benzalkonium chloride was well known as an acceptable preservative for use with an azelastine nasal spray?

2. Before 1985, did you have any experience in formulating nasal sprays? If so, please describe your experience in formulating nasal sprays.

3. Please generally describe your involvement in assisting Asta Pharma AG in obtaining the German '681 patent?

4. Please generally describe your involvement in assisting Asta Pharma AG in obtaining the U.S. '194 Patent?

MM. Development of Azelastine Nasal Spray

1. To your knowledge, was Asta Pharma AG working with any other companies on the formulation of azelastine medicaments? If so, who was Asta Pharma AG working with and when?

2. What was the relationship between Asta Pharma AG and Carter Wallace/Eisai regarding new drug formulations using azelastine?

3. When did you first learn that others were working on formulations of azelastine for topical administration? Who did you understand was working on the formulations of azelastine for topical administration?

4. What involvement, if any, did you have with Carter Wallace regarding the formulation of azelastine nasal sprays? Please describe your involvement with Carter Wallace on the formulation of azelastine nasal sprays.

NN. Miscellaneous Issues

1. At the time you developed the azelastine nasal spray, what other nasal spray products were on the market for the treatment of allergy-related rhinitis, normal common colds and the vasomotor cold? What were the names of the products and who were the manufacturers? If you know, what were the formulations of the various nasal sprays on the market at the time you developed the azelastine nasal spray?

2. At the time you developed the azelastine nasal spray, did Asta Pharma AG have any nasal sprays on the market for the treatment of allergy-related rhinitis, normal common colds and the vasomotor cold? If so, what was the product and what was its active ingredients?

3. Is your azelastine nasal spray formulation the first nasal spray developed

and offered by Asta Pharma AG or related companies for the treatment of allergy-related rhinitis, normal common colds and the vasomotor cold?

4. Is your azelastine eye drop formulation the first eye drop formulation developed and offered by Asta Pharma AG or related companies for the treatment of allergy-related rhinitis, normal common colds and the vasomotor cold?

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EXHIBIT 2

List of Exhibits for Mr. Helmet Hettche

1. German Patent Application P 37 38 681.6 (MP0029-MP0049)
2. U.S. Patent No. 5,164,194
3. European Patent No. 0 316 633
4. Decision of the Opposition Division of the European Patent Office mailed March 28, 1996 (with English translation)
5. Decision of the Technical Court of Appeals 3.3.2 dated April 5, 2000 (with English translation).
6. Offenlegungsschrift 21 64 058 (with English translation).
7. U.S. Patent No. 3,813,384 (with German translation).
8. December 1982 Asta-Werke AG Toxicology Report (with German translation) (ATI00001105)
9. Abstract 76, Chand N., Nolan K., Diamantis W., Sofia R.D. (1985) *Pharmacologist*; 27:162 (with German translation).
10. Single page document with box drawn around text "Beispiel 24" (AS-MEDA0001568).
11. Internal Letter dated September 6, 1985 from Dr. Aurich to Prof. Dr. Breuel (AS-MEDA0000601-602) (with English translation)
12. Notice to Dr. Herbst prepared by Dr. Hettche and dated January 27, 1986.
13. Internal Memo prepared by Dr. Hettche to Dr. Herbst dated August 13, 1990 (AS-MEDA0001345 (with English translation).
14. Handwritten note by Dr. Hettche dated February 18, 1986 (AS-MEDA0001938) (with English translation).
15. Handwritten note by Dr. Hettche to Dr. Ulbrich dated August 12, 1987 (AS-MEDA0000600).
16. U.S. Patent No. 4,704,387 (with German translation).
17. German Patent No. 3,539,873 (with English translation).
18. German Patent No. 3,433,776 (with English translation).

19. O. Keanz, "Vademecum," 12th Revised Edition (AS-MEDA0000617-629) (with English Translation).

20. Breuninger H. (1971) *HNO*, 1971 Mar;19(3):65-8.

21. Antistin-Privin package insert.

22. Single page 725 taken from a reference involving "Medications for the eye, ear and nose" and produced as AS-MEDA0007755 (with English translation).

23. H.J.M. van de Donk, et al., "The effects of nasal drops on the ciliary beat frequency of chicken embryo tracheas." Rhinology 19, 215-230, 1981.

24. Aberer W., Tappeiner G. (1988) *Wiener klinische Wochenschrift*, 1988 Dec. 2; 100(23):763-765.

25. Report dated September 13, 1988 (AS-MEDA0003522-3525).

26. Declaration of Dr. Szelenyi dated January 23, 1990 (with German translation).

27. Document entitled "Inhibition of allergic histamine release from rat peritoneal mast cells" attached as part of Dr. Szelenyi's January 23, 1990 Declaration.

28. Declaration of Dr. Istvan Szelenyi dated June 1, 1990 (with German translation).

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